

DETAILED ACTION

Status of the Application

- [1] Claims 77-85 are pending in the application.
- [2] Applicant's amendment to the claims, filed on 9/8/09, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.
- [3] Applicant's remarks filed on 9/8/09 in response to the non-final rejection mailed on 3/9/09 have been fully considered and are deemed to be persuasive to overcome at least one of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [4] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, First Paragraph

- [5] The scope of enablement rejection of claims 77-80 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the instant amendment to claim 77 to limit the amino acid produced by the claimed method to L-homoserine, L-threonine, and branched chain L-amino acids.

Claim Rejections - 35 USC § 103

- [6] The rejection of claims 77-84 under 35 U.S.C. 103(a) as being unpatentable over Debabov in view of Vrljic, Database Accession Number P27846, Daniels, and Kobayashi and as evidenced by Zakataeva is maintained for the reasons of record and

the reasons set forth below. The rejection was fully explained in a prior Office action.

See item 10 beginning at p. 7 of the Office action mailed on 3/9/09.

RESPONSE TO ARGUMENT: At p. 6 of the instant remarks, applicant requests clarification regarding the reference of Daniels et al. (*Science* 257:771-778, 1992) as being filed with the IDS of 1/26/07. As noted in the accompanying interview summary, the examiner was under the impression that the Daniels et al. reference was already of record in the application file. Because the references have the same first author and similar titles, the examiner inadvertently read the Daniels et al. citation, AW, in the PTO-1449 mailed on 11/2/01 as being the same as Daniels et al. (*Science* 257:771-778, 1992), cited in the obviousness rejections. However, upon further review, it is apparent that the two references are not the same. Since a copy of Daniels et al. (*Science* 257:771-778, 1992) was not made available to applicant with the prior Office action, a copy of that reference is attached hereto and in the interest of customer service, this Office action is non-final. If applicant identifies further inconsistencies in this or a future Office communication, applicant is urged to contact the examiner by telephone to quickly resolve the issue(s) and expedite prosecution of the application.

Turning now to the merits of applicant's arguments, beginning at p. 6 of the instant remarks, applicant argues: 1) Debabov and Vrljic are silent with respect to SEQ ID NO:3; 2) neither Database Accession Number P27846 nor Kobayashi provides an expectation of achieving expression of a functional protein that will enhance L-threonine efflux; 3) Kobayashi does not teach a method of L-amino acid production; and 4) evidentiary reference Zakataeva fails to disclose L-amino acid production using the *rhtC*

gene or increased L-amino acid production by using an *E. coli* overexpressing the disclosed RhtC polypeptide.

Applicant's argument is not found persuasive. The examiner maintains the position that the claimed invention would have been obvious to one of ordinary skill in the art at the time of the invention.

There appears to be no dispute that Database Accession Number P27846 annotates the disclosed polypeptide as a threonine efflux protein, that the polypeptide disclosed by Database Accession Number P27846 is encoded by SEQ ID NO:3 herein, and that Kobayashi teaches a polynucleotide encoding the polypeptide of Database Accession Number P27846. What appears to be in dispute is whether or not the prior art provides motivation to transform an *E. coli* bacterium with a nucleic acid encoding the polypeptide of Database Accession Number P27846 and use of the resulting transformant in the L-amino acid production method of Debabov. The examiner maintains that the teachings of the prior art, when taken as a whole, provide clear motivation for combining the references. The motivation is substantially based on the references of Vrljic and Database Accession Number P27846. As noted in the prior Office action at p. 13, the reference of Vrljic suggests increasing expression of an L-amino acid exporter protein for a desired L-amino acid in order to achieve enhanced accumulation of the L-amino in the culture medium. While it is acknowledged there is no *in vitro* or *in vivo* experimental evidence in the cited references that the polypeptide of Database Accession Number P27846 has threonine export activity, the reference of Database Accession Number P27846 annotates the polypeptide as a threonine export

protein and there is no evidence of record to suggest otherwise to an ordinarily skilled artisan at the time of the invention. Although applicant argues there is no evidence in the cited references that the polypeptide of Database Accession Number P27846 would be functional, it is noted that there is also *no* evidence that the polypeptide would *not* be functional.

At the time of the invention, *E. coli* was well-known as being used in the bioproduction of L-threonine as shown by Debabov. Also, transformation of an *E. coli* with a polynucleotide for overexpression of a desired protein was well-known and routinely practiced. As such, because *E. coli* was used in the bioproduction of L-threonine as shown by Debabov, the protein of Database Accession Number P27846 was annotated as an L-threonine export protein, and only routine experimentation was required to transform an *E. coli* bacterium with a nucleic acid encoding the polypeptide of Database Accession Number P27846, one would have been motivated to use an *E. coli* overexpressing the polypeptide of Database Accession Number P27846 in the method of Debabov. Also, since only routine experimentation is required, one of ordinary skill in the art would have had a reasonable expectation of success to transform an *E. coli* with a polynucleotide for overexpression of the polypeptide of Database Accession Number P27846 and to use such transformant in the method of Debabov. This is all that is required to satisfy the claim limitations – *no a priori* knowledge of whether or not the polypeptide of Database Accession Number P27846 is functional is required to practice this method.

At least for the reasons of record and the reasons set forth above, the examiner maintains the position that the claimed invention would have been obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

[7] Status of the claims:

Claims 77-85 are pending.

Claims 77-84 are rejected.

Claim 85 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claim 85 is free of the prior art of record because the examiner can find no teaching or suggestion in the prior art of record that the YigJ polypeptide of Database Accession Number P27846 has L-valine or L-leucine transport activity.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/David J. Steadman/
Primary Examiner, Art Unit 1656